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Signature:

(Anna P. Lucey)

Docket No.: CWRU-P01-018  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Grimpe et al.

Examiner: Not Yet Assigned

Application No.: 10/698190

Confirmation No.: 1183

Filed: October 31, 2003

Art Unit: 1632

For: METHODS OF INHIBITING GLIAL SCAR  
FORMATION

**INFORMATION DISCLOSURE STATEMENT (IDS)**

Commissioner for Patents  
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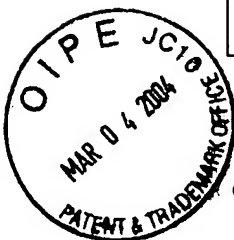
Dear Sir:

Pursuant to 37 CFR 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 CFR 1.97(b)(3)).

Copies of each foreign patent and journal cited on PTO/SB/08 are attached.

While the information and references disclosed in this Information Disclosure Statement may be "material" pursuant to 37 CFR 1.56, it is not intended to constitute an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such (37 CFR 1.97(h)).



In accordance with 37 CFR 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR 1.56(a) exists. Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents should one or more of the documents be applied against the claims of the present application.

It is submitted that the Information Disclosure Statement is in compliance with 37 CFR 1.98 and the Examiner is respectfully requested to consider the listed references.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 18-1945, under Order No. CWRU-P01-018.

Dated:

Respectfully submitted,

By 

Melissa S. Rones, Ph.D.

Registration No.: 54,408

ROPES & GRAY LLP

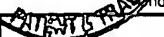
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**Complete if Known**

Application Number	10/698190
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Filing Date	October 31, 2003
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First Named Inventor	Barbara Grimpe
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Art Unit	1632
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Examiner Name	Not Yet Assigned
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Attorney Docket Number	CWRU-P01-018
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Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)	MM-DD-YYYY		
	AA	5,093,246	03-03-1992	Cech et al.	
	AB	5,807,718	09-15-1998	Joyce et al.	
	AC	6,110,462	08-29-2000	Barbas et al.	

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Type of Document
		Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)	MM-DD-YYYY			
	AD ✓	WO 88/04300-A1	06-16-1988	University Patents, Inc.		
	AE ✓	WO 90/11364-A1	10-04-1990	University Patents, Inc.		
	AF ✓	WO 99/08533-A1	02-25-1999	Yale University		
	AG ✓	WO 01/49831-A2	07-12-2001	Kleesiek		

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Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	AH	Asher, R.A. et al. Neurocan is Upregulated in Injured Brain and in Cytokine-Treated Astrocytes. J. Neurosci. 20(7), 2427-2438 (1 April 2000).	
	AI	Bai, X. et al. Chinese Hamster Ovary Cell Mutants Defective in Glycosaminoglycan Assembly and Glucuronosyltransferase I. J. Biol. Chem. 274(19), 13017-24 (7 May 1999).	
	AJ	Bamber, N.I. et al. Neurotrophins BDNF and NT-3 promote axonal re-entry into the distal host spinal cord through Schwann cell-seeded mini-channels. Euro. J. Neurosci. 13, 257-68 (2001).	
	AK	Been, M.D. and Cech, T.R. One Binding Site Determines Sequence Specificity of Tetrahymena Pre-rRNA Self-Splicing, Trans-Splicing, and RNA Enzyme Activity. Cell 47, 207-16 (24 Oct. 1986).	
	AL	Benn, S.C. et al. Hsp27 Upregulation and Phosphorylation is Required for Injured Sensory and Motor Neuron Survival. Neuron 36, 45-56 ((26 Sept. 2002).	
	AM	Borisoff, J.F. et al. Suppression of Rho-kinase activity promotes axonal growth on inhibitory CNS substrates. Mol. Cell. Neurosci. 22, 405-416 (2003).	
	AN	Bradbury, E.J. et al. Chondroitinase ABC promotes functional recovery after spinal cord injury. Nature 416, 636-40 (11 April 2002).	

Examiner  
Signature

Date	
Considered	

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Sheet	4	of	6	Attorney Docket Number	CWRU-P01-018

BV	Koslowski, R. et al. Changes in xylosyltransferase activity and in proteoglycan deposition in bleomycin-induced lung injury in rat. Eur. Respir. J. 18, 347-356 (2001).
BW	Kozlova, E.N. et al. Peripherally grafted human foetal dorsal root ganglion cells extend axons into the spinal cord of adult host rats by circumventing dorsal root entry zone astrocytes. NeuroReport 6, 269-272 (1995).
BX	Kuhn, J. et al. First Isolation of Human UDP-D-Xylose: Proteoglycan Core Protein Beta-D-Xylosyltransferase Secreted from Cultured JAR Choriocarcinoma Cells. J. Biol. Chem. 276(7), 4940-4947 (16 Feb. 2001).
BY	Lakatos, A. et al. Olfactory Ensheathing Cells and Schwann Cells Differ in Their In Vitro Interactions with Astrocytes. GLIA 32, 214-225 (2000).
BZ	Lal, P.G. et al. Astrocytoma and Schwann Cells in Coculture. Mol. Chem. Neuropathol. 29, 93-104 (1996).
CA	Lee, J.C. et al. Gliogenesis in the Central Nervous System. GLIA 30, 105-121 (2000).
CB	Liuzzi, F.J. and Lasek, R.J. Astrocytes Block Axonal Regeneration in Mammals by Activating the Physiological Stop Pathway. Science 237, 642-645 (7 Aug. 1987).
CC	Margolis, R.U. and Margolis, R.K. Chondroitin sulfate proteoglycans as mediators of axon growth and pathfinding. Cell Tissue Res. 290, 343-348 (1997).
CD	Martin, R.C. et al. A Gene Encoding the Cytokinin Enzyme Zeatin O-Xylosyltransferase of Phaseolus vulgaris. Plant Physiology 120, 553-557 (June 1999).
CE	Maurel, P. et al. Phosphacan, a chondroitin sulfate proteoglycan of brain that interacts with neurons and neural cell-adhesion molecules, is an extracellular variant of a receptor-type protein tyrosine phosphatase. PNAS 91, 2512-2516 (March 1994).
CF	McKeon, R.J. et al. Injury-Induced Proteoglycans Inhibit the Potential for Laminin-Mediated Axon Growth on Astrocytic Scars. Exp. Neurol. 136, 32-43 (1995).
CG	McKeon, R.J. et al. The Chondroitin Sulfate Proteoglycans Neurocan and Phosphacan Are Expressed by Reactive Astrocytes in the Chronic CNS Glial Scar. J. Neurosci. 19(24), 10778-10788 (15 Dec. 1999).
CH	Menei, P. et al. Schwann cells genetically modified to secrete human BDNF promote enhanced axonal regrowth across transected adult rat spinal cord. Eur. J. Neurosci. 10, 607-621 (1998).
CI	Neumann, S. and Woolf, C.J. Regeneration of Dorsal Column Fibers into and beyond the Lesion Site following Adult Spinal Cord Injury. Neuron 23, 83-91 (May 1999).
CJ	Neumann, S. et al. Regeneration of Sensory Axons within the Injured Spinal Cord Induced by Intraganglionic cAMP Elevation. Neuron 34, 885-893 (13 June 2002).
CK	Nomura, H. et al. Dorsal root rupture injury induces extension of astrocytic processes into the peripheral nervous system and expression of GDNF in astrocytes. Brain Res. 950, 21-30 (2002).
CL	Oudega, M. and Hagg, T. Neurotrophins promote regeneration of sensory axons in the adult rat spinal cord. Brain Res. 818, 431-438 (1999).

Examiner Signature		Date Considered	
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Sheet	3	of	6	Attorney Docket Number	CWRU-P01-018

BE	Garwood, J. et al. DSD-1-Proteoglycan is the Mouse Homolog of Phosphacan and Displays Opposing Effects on Neurite Outgrowth Dependent on Neuronal Lineage. J. Neurosci. 19(10), 3888-3899 (15 May 1999).
BF	Ghirnikar, R.S. and Eng, L.F. Chondroitin Sulfate Proteoglycan Staining in Astrocyte-Schwann Cell Co-cultures. GLIA 14, 145-152 (1995).
BG	Golding, J.P. et al. An in Vitro Model of the Rat Dorsal Root Entry Zone Reveals Developmental Changes in the Extent of Sensory Axon Growth into the Spinal Cord. Mol. Cell. Neurosci. 7, 191-203 (1996).
BH	Golding, J.P. et al. Behaviour of DRG Sensory Neurites at the Intact and Injured Adult Rat Dorsal Root Entry Zone: Postnatal Neurites Become Paralysed, Whilst Injury Improves the Growth of Embryonic Neurites. GLIA 26, 309-323 (1999).
BI	Gotting, C. et al. Xylosylation of Alternatively Spliced Isoforms of Alzheimer APP by Xylosyltransferase. J. Prot. Chem. 17(3), 295-302 (1998).
BJ	Gotting, C. et al. Serum Xylosyltransferase: a New Biochemical Marker of the Sclerotic Process in Systemic Sclerosis. J. Invest. Dermatol. 112, 919-924 (1999).
BK	Gotting, C. et al. Elevated Serum Xylosyltransferase Activity Correlates with a High Level of Hyaluronate in Patients with Systemic Sclerosis. Acta Derm. Venerol. 80, 60-61 (2000).
BL	Gotting, C. et al. Molecular Cloning and Expression of Human UDP-D-Xylose: Proteoglycan Core Protein Beta-D-Xylosyltransferase and its First Isoform XT-11. J. Mol. Biol. 304, 517-528 (2000).
BM	Gotting, C. et al. Xylosyltransferase activity in seminal plasma of infertile men. Clinica Chimica Acta 317, 199-202 (2002).
BN	Grumet, M. et al. Functional Characterization of Chondroitin Sulfate Proteoglycans of Brain: Interactions with Neurons and Neural Cell Adhesion Molecules. J. Cell Biol. 120, 815-824 (Feb. 1993).
BO	Grumet, M. et al. Functions of Brain Chondroitin Sulfate Proteoglycans During Development: Interactions with Adhesion Molecules. Perspectives on Dev. Neurobiol. 3, 319-330 (1996).
BP	Haas, C.A. et al. Entorhinal Cortex Lesion in Adult Rats Induces the Expression of the Neuronal Chondroitin Sulfate Proteoglycan Neurocan in Reactive Astrocytes. J. Neurosci. 19(22), 9953-9963 (15 Nov. 1999).
BQ	Haseloff, J. and Gerlach, W.L. Simple RNA enzymes with new and highly specific endoribonuclease activities. Nature 334, 585-591 (18 Aug. 1988).
BR	Hoffman-Kim, D. et al. Patterns of Chondroitin Sulfate Immunoreactivity in the Developing Tectum Reflect Regional Differences in Glycosaminoglycan Biosynthesis. J. Neurosci. 18(15), 5881-5890 (1 Aug. 1998).
BS	Hoffmann, H.-P. et al. Location of Xylosyltransferase in the Cisternae of the Rough Endoplasmic Reticulum of Embryonic Cartilage Cells. Connective Tissue Res. 12, 151-163 (1984).
BT	Kearns, A.E. et al. Initiation of Chondroitin Sulfate Biosynthesis: A Kinetic Analysis of UDP-D-Xylose: Core Protein Beta-D-Xylosyltransferase. Biochemistry 30, 7477-7483 (1991).
BU	Kitagawa, H. et al. Molecular Cloning and Expression of Glucuronyltransferase I Involved in the Biosynthesis of the Glycosaminoglycan-Protein Linkage Region of Proteoglycans. J. Biol. Chem. 273(12), 6615-6618 (20 March 1998).

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AO	Bunge, M.B. and Kleitman, N. Neurotrophins and Neuroprotection Improve Axonal Regeneration into Schwann Cell Transplants Placed in Transected Adult Rat Spinal Cord. In: CNS Regeneration: Basic Science and Clinical Aspects. Tuszinski, M.H. and Kordower, J., eds., San Diego: Academic Press, pp. 631-646, (1999).
AP	Bunge, M.B. Bridging the transected or contused adult rat spinal cord with Schwann cell and olfactory ensheathing glia transplants. Progress in Brain Research, Vol. 137, Ch. 19, L. McKerracher et al., eds. (2002).
AQ	Cai, D. et al. Arginase I and Polyamines Act Downstream from Cyclic AMP in Overcoming Inhibition of Axonal Growth MAG and Myelin in Vitro. Neuron 35, 711-719 (15 Aug. 2002).
AR	Carlstedt, T. Nerve fibre regeneration across the peripheral-central transitional zone. J. Anat. 190, 51-56 (1997).
AS	Chen, M.S. et al. Nogo-A is a myelin-associated neurite outgrowth inhibitor and an antigen for monoclonal antibody IN-1. Nature 403, 434-439 (27 Jan. 2000).
AT	Cheng, C. and Zochodne, D.W. In Vivo Proliferation, Migration and Phenotypic Changes of Schwann Cells in the Presence of Myelinated Fibers. Neurosci. 115, 321-329 (2002).
AU	Chong, M.S. et al. Intrinsic Versus Extrinsic Factors in Determining the Regeneration of the Central Processes of Rat Dorsal Root Ganglion Neurons: The Influence of a Peripheral Nerve Growth. J. Comp. Neurol. 370, 97-104 (1996).
AV	Chong, M.S. et al. Axonal Regeneration From Injured Dorsal Roots Into the Spinal Cord of Adult Rats. J. Comp. Neurol. 410, 42-54 (1999).
AW	Condic, M.L. Adult Neuronal Regeneration Induced by Transgenic Integrin Expression. J. Neurosci. 21(13), 4782-88 (1 July 2001).
AX	Davies, S.J.A. et al. Regeneration of adult axons in white matter tracts of the central nervous system. Nature 390, 680-683 (Dec. 1997).
AY	Davies, S.J.A. et al. Robust Regeneration of Adult Sensory Axons in Degenerating White Matter of the Adult Rat Spinal Cord. J. Neurosci. 19(14), 5810-5822 (15 July 1999).
AZ	Dergham, P. et al. Rho Signaling Pathway Targeted to Promote Spinal Cord Repair. J. Neurosci. 22(15), 6570-6577 (1 Aug. 2002).
BA	Eddleston, M. and Mucke, L. Molecular Profile of Reactive Astrocytes: Implications for Their Role in Neurologic Disease. Neurosci. 54, 15-36 (1993).
BB	Fidler, P.S. et al. Comparing Astrocytic Cell Lines that are Inhibitory or Permissive for Axon Growth: the Major Axon-Inhibitory Proteoglycan is NG2. J. Neurosci. 19(20), 8778-8788 (15 Oct. 1999).
BC	Fitch, M.T. et al. Cellular and Molecular Mechanism of Glial Scarring and Progressive Cavitation: In Vivo and In Vitro Analysis of Inflammation-Induced Secondary Injury after CNS Trauma. J. Neurosci. 19(19), 8182-8198 (1 Oct. 1999).
BD	Friedlander, D.R. et al. The Neuronal Chondroitin Sulfate Proteoglycan Neurocan Binds to the Neural Cell Adhesion Molecules Ng-CAM/L1/NILE and N-CAM, and Inhibits Neuronal Adhesion and Neurite Outgrowth. J. Cell Biol. 125, 669-680 (1994).

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CM	Pfeil, U. and Wenzel, K.-W. Purification and some properties of UDP-xylosyltransferase of rat ear cartilage. <i>Glycobiology</i> 10(8), 803-807 (2000).
CN	Pindzola, R.R. et al. Putative Inhibitory Extracellular Matrix Molecules at the Dorsal Root Entry Zone of the Spinal Cord during Development and after Root and Sciatic Nerve Lesions. <i>Dev. Biol.</i> 156, 34-48 (1993).
CO	Qiu, J. et al. Glial Inhibition of Nerve Regeneration in the Mature Mammalian CNS. <i>GLIA</i> 29, 166-174 (2000).
CP	Qiu, J. et al. Spinal Axon Regeneration Induced by Elevation of Cyclic AMP. <i>Neuron</i> 34, 895-903 (13 June 2002).
CQ	Ramer, M.S. et al. Neurotrophin-3-Mediated Regeneration and Recovery of Proprioception Following Dorsal Rhizotomy. <i>Mol. Cell. Neurosci.</i> 19, 239-249 (2002).
CR	Ramon-Ceuto, A. and Nieto-Sampedro, M. Regeneration into the Spinal Cord of Transected Dorsal Root Axons is Promoted by Ensheathing Glia Transplants. <i>Exp. Biol.</i> 127, 232-244 (1994).
CS	Rohrmann, K. et al. Two N-acetylgalactosaminyltransferase are involved in the biosynthesis of chondroitin sulfate. <i>Eur. J. Biochem.</i> 148, 463-469 (1985).
CT	Romero, M.I. et al. Functional Regeneration of Chronically Injured Sensory Afferents in to Adult Spinal Cord after Neurotrophin Gene Therapy. <i>J. Neurosci.</i> 21(2), 8408-8416 (1 Nov. 2001).
CU	Santoro, S.W. and Joyce, G.F. A general purpose RNA-cleaving DNA enzyme. <i>PNAS</i> 94, 4262-4266 (April 1997).
CV	Sarver, N. et al. Ribozymes as Potential Anti-HIV-1 Therapeutic Agents. <i>Science</i> 247, 1222-1225 (9 March 1990).
CW	Silver, J. Inhibitory molecules in development and regeneration. <i>J. Neurol.</i> 241, S22-S24 (1994).
CX	Snow, D.M. et al. Sulfated Proteoglycans in Astroglial Barriers Inhibit Neurite Outgrowth in Vitro. <i>Exp. Neurol.</i> 109, 111-130 (1990).
CY	Snow, D.M. et al. Binding Characteristics of Chondroitin Sulfate Proteoglycans and Laminin-1, and Correlative Neurite Outgrowth Behaviors in a Standard Tissue Culture Choice Assay. <i>J. Neurobiol.</i> 51, 285-301 (2002).
CZ	Stichel, C.C. and Muller, H.W. The CNS lesion scar: new vistas on an old regeneration barrier. <i>Cell Tissue Res.</i> 294, 1-9 (1998).
DA	Sun, L.-Q. et al. Suppression of Smooth Muscle Cell Proliferation by a c-myc RNA-cleaving Deoxyribozyme. <i>J. Biol. Chem.</i> 274(24), 17236-17241 (1999).
DB	Takami, T. et al. Schwann Cell but not Olfactory Ensheathing Glia Transplants Improve Hindlimb Locomotor Performance in the Moderately Contused Adult Rat Thoracic Spinal Cord. <i>J. Neurosci.</i> 22(15), 6670-6681 (1 Aug. 2002).
DC	Tone, Y. et al. Characterizations of recombinant human glucuronyltransferase I involved in the biosynthesis of the glycosaminoglycan-protein linkage region of proteoglycans. <i>FEBS Letters</i> 459, 415-420 (1999).

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	DD ✓	Tsuchida, K. et al. Purification and characterization of fetal bovine serum Beta-N-acetyl-D-galactosaminyltransferase and Beta-D-glucuronyltransferase involved in chondroitin sulfate biosynthesis. Eur. J. Biochem. 264, 461-467 (1999).	
	DE ✓	Uchimura, K. et al. Functional Analysis of the Chondroitin 6-Sulfotransferase Gene in Relation to Lymphocyte Subpopulations, Brain Development, and Oversulfated Chondroitin Sulfates. J. Biol. Chem. 277(2), 1443-1450 (11 Jan. 2002).	
	DF ✓	Uyama, T. et al. Molecular Cloning and Expression of Human Chondroitin N-Acetylgalactosaminyltransferase. J. Biol. Chem. 277(11), 8841-8846 (15 March 2002).	
	DG ✓	Weilke, C. et al. Determination of xylosyltransferase activity in serum with recombinant human bikunin as acceptor. Clin. Chem. 43, 45-51 (1997).	
	DH ✓	Wilson, I.B.H. Functional Characterization of Drosophila melanogaster Peptide O-Xylosyltransferase, the Key Enzyme for Proteoglycan Chain Initiation and Member of the Core 2/I N-Acetylglucosaminyltransferase Family. J. Biol. Chem. 277(24), 21207-21212 (14 June 2002).	
	DI ✓	Yu, X. and Bellamkonda, R.V. Dorsal Root Ganglia Neurite Extension is Inhibited by Mechanical and Chondroitin Sulfate-Rich Interfaces. J. Neurosci. Res. 66, 303-310 (2001).	
	DJ ✓	Zaug, A.J. et al. A Labile Phosphodiester Bond at the Ligation Junction in a Circular Intervening Sequence RNA. Science 224, 574-578 (11 May 1984).	
	DK ✓	Zaug, A.J. et al. The Tetrahymena ribozyme acts like an RNA restriction endonuclease. Nature 324, 429-433 (4 Dec. 1986).	
	DL ✓	Zaug, A.J. and Cech, T.R. The Intervening Sequence RNA of Tetrahymena is an Enzyme. Science 231, 470-475 (31 Jan. 1986).	
	DM ✓	Zhang, Y. et al. Expression of CHL1 and L1 by Neurons and Glia Following Sciatic Nerve and Dorsal Root Injury. Mol. Cell. Neurosci. 16, 71-86 (2000).	
	DN ✓	Zhang, Y. et al. Correlation between Putative Inhibitory Molecules at the Dorsal Root Entry Zone and Failure of Dorsal Root Axonal Regeneration. Mol. Cell. Neurosci. 17, 444-459 (2001).	
	DO ✓	Brinkmann, T. et al. Recognition of Acceptor Proteins by UDP-D-xylose Proteoglycan Core Protein Beta-D-Xylosyltransferase. J. Biol. Chem. 272(17), 11171-11175 (25 April 1997).	

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<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>Applicant is to place a check mark here if English language Translation is attached.

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